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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/973,576	04/02/98	MALFROY-CAMINE B	15390-000130

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ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 08/973,576	Applicant(s) Malfroy-Camine
	Examiner Ron Schwadron, Ph.D.	Group Art Unit 1644

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-23* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-23* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

15. 35 U.S.C. § 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

16. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

17. Claim 23 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 23 of copending application Serial No. 08/482116. The two claims are identical.

18. The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 14-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1,2,4-12,24,29-33 of

copending application Serial No. 08/483,944. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. While the two sets of claims differ in scope, both sets of claims encompass methods which make the same products and compositions which contain the same ingredients. Therefore, the two sets of claims under consideration in this rejection would have been prima facie obvious in view of each other to one of ordinary skill in the art at the time the invention was made for the aforementioned reasons.

20. Claims 1-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of copending application Serial No. 08/482116. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. While the two sets of claims differ in scope, both sets of claims encompass the same products and methods which make and use the same products and compositions which contain the same ingredients. Therefore, the two sets of claims under consideration in this rejection would have been prima facie obvious in view of each other to one of ordinary skill in the art at the time the invention was made for the aforementioned reasons.

21. Claim 23 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-22 of copending application Serial No. 08/482116. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. While the two sets of claims differ in scope, it would have been obvious to use the products disclosed in claims 1-22 of copending application Serial No. 08/482116 in any art recognized immunoassay. Therefore, the two sets of claims under consideration in this rejection would have been prima facie obvious in view of each other to one of ordinary skill in the art at the time the invention was made for the aforementioned reasons.

22. Claims 1-23 are under consideration.

23. The oath or declaration is defective. A new oath or declaration in compliance with 37 C.F.R. § 1.67(a) identifying this application by its Serial Number and filing date is required. See M.P.E.P. §§ 602.01 and 602.02.

The oath or declaration is defective because:
The declaration is defective because the declaration needs to claim priority to US application 08/482116 under 35 U.S.C. § 120. A substitute declaration is required.

24. Drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

25. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application (eg. 08/482116), specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of non-provisional application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

26. Applicant needs to update the status of all US Patent applications (eg. abandoned, etc.) disclosed in the specification (eg. page 3).

27. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825, however, this application fails to comply with the requirements for patent applications containing nucleotide sequence and/or amino acid sequence disclosures.

Applicant is required to fulfill these requirements by defining the SEQ ID NOS in the specification. The following procedure is to be used for cases that contain the same sequence disclosure as the parent. The applicant need not submit a new computer readable form of the Sequence Listing for this CIP application. However, (1) the specification must contain a paper copy of the Sequence Listing, (2) applicant must request in writing that the CRF in the parent case be used to prepare a file for the offspring and (3) applicant must submit a statement that the paper copy of the Sequence Listing in the offspring is identical to the computer readable form submitted in the

parent case.

It is valid to use this approach to bring sequences into rule 60 continuation, divisional or CIPs as long as there are no new sequences (as per this application).

28. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

29. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabling for the claimed method wherein the characteristics of a protein are "modified". The claimed invention encompasses a method wherein the binding affinity, avidity or immunogenicity of the antibodies made by the claimed method are modified. The art recognizes that binding affinity of antibodies is mediated by the amino acid sequence of CDRs found in the V region of antibodies (eg. see Harris et al.). The claimed method does not modify the amino acid sequence of CDRs found in the V region of antibodies and thus would be expected to have no effect on binding affinity. There is no disclosure in the specification that the binding affinity, avidity or immunogenicity of the antibodies made by the claimed method are modified. Therefore, the specification is not enabling for the claimed invention.

30. Claims 14-22 rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14-22 are indefinite in that they read on compositions, but claim compounds. The claims need to recite additional ingredients (eg. buffer) that would render these claims compositions instead of compounds. Claim 19 is indefinite in the recitation of "prophylaxis" because it is unclear what this encompasses in the context recited in the claim. Claim 20 is indefinite in the recitation of "diagnostic reporter" because it is unclear what this means or

encompasses. Claim 22 is indefinite in that it is a dependent claim that depends on itself.

31. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

32. Claims 1-23 are rejected under 35 U.S.C. § 103 as being unpatentable over Kabanov et al. (pages 33-36) or Kabanov et al. (pages 63-67) in view of Bischofberger et al. and Rodwell et al.

The claims are drawn to lipidized proteins comprising a polypeptide covalently linked to a lipid through a carbohydrate moiety, a method for making said conjugates, compositions containing said lipidized proteins and a method of diagnosis using said proteins. Kabanov et al. teach lipidized proteins (including antibodies) and methods for making said proteins (see entire document, either reference). Kabanov et al. do not teach that the lipidized proteins comprise a polypeptide covalently linked to a lipid through a carbohydrate moiety. Bischofberger et al. teach that an aminolipid (lipoamine) can be used for attaching a lipid to an immunoconjugate (page 13, paragraph three). A routineer would have realized that said method could have also been used to attach said lipid to an oxidized antibody saccharide, because Rodwell et al. teach that amine containing compounds (e.g. lipoamine) can be attached to antibodies by oxidation of antibody saccharides to aldehydes which can react with amine containing compounds (page 2635, first column, second sentence, *Discussion* section). Bischofberger et al. teaches a wide variety of lipids can be used in the invention (page 4, third paragraph), and coupled with his previous teaching of a lipoamine for lipid conjugates, a routineer would have derived the lipoamine compounds of claims 4-6. A routineer would have applied the instant method to any glycoprotein. The antibodies taught by Kabanov et al. consist of mu or gamma heavy chains and is coded for by an immunoglobulin superfamily gene. A routineer would have used the instant method to lipidize monoclonal antibodies. A routineer would have used the instant method to produce lipidized proteins or antibodies. It would have been prima facie obvious to one of ordinary skill in the art

at the time the invention was made to have created the claimed inventions because Kabanov et al. teach lipidized proteins (including antibodies) and methods for making said proteins, Bischofberger et al. teach that an aminolipid (lipoamine) can be used for attaching a lipid to an immunoconjugate and a routineer would have realized that said method could have also been used to attach said lipid to an oxidized antibody saccharide, because Rodwell et al. teach that amine containing compounds (e.g. lipoamine) can be attached to antibodies by oxidation of antibody saccharides to aldehydes which can react with amine containing compounds. A routineer would have lipidized antibodies which bind intracellular proteins because the major purpose of the invention is to deliver proteins intracellularly. One of ordinary skill in the art would have been motivated to do the aforementioned because Kabanov et al. teaches lipidized antibodies and Rodwell et al. teaches the advantages of preparing antibody conjugates via oligosaccharide linkage (see abstract). Kabanov et al. teach that lipidized antibodies can be used to target intracellular proteins (see pages 65-67). A routineer would have administered said lipidized antibody in vivo in a pharmaceutical composition. Kabanov et al. teach lipidized antibody against viral protein (see page 65). A routineer would have prepared lipidized antibody against any art known viral protein. Based on the teachings of Kabanov et al., it would have been obvious to a routineer that lipidized antibodies could have been used in any art known assay (eg. immunoassay) that conventional antibodies were used, wherein it was desirable to detect intracellular antigens (eg. viral antigens). Labeled antibodies for use in immunoassays are well known in the art.

33. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

34. Claims 1-3,7,8,14,15,19,20,23 are rejected under 35 U.S.C. 102(e) as being anticipated

by Horan et al. (US Patent 5,665,328).

Horan et al. teach lipidized glycoproteins including antibodies wherein the carbohydrate side chain of the glycoprotein is oxidized and a lipophilic amine is reacted to form a lipidized protein (see column 14, lines 39-46) and column 5, second paragraph. Horan et al. teach that said lipidized proteins can contain a radionucleotide (see column 7, second paragraph). Horan et al. teach compositions containing lipidized protein and a pharmaceutically acceptable carrier. Horan et al. teach that the lipidized protein is made as per the methods of claim 1-3 (see column 14, lines 39-46). Antibodies are naturally occurring glycoproteins that are members of the immunoglobulin superfamily. Horan et al. teach the use of monoclonal antibodies in the claimed invention (see column 5, second paragraph).

35. Claims 1-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Malfroy-Camine (WO 94/01131).

Regarding priority for the claimed invention, the instant application currently only claims priority to US application 08/482116, filed 6/7/95. Malfroy-Camine (WO 94/01131) teach the claimed invention (see claims and pages 1-45).

36. Claims 1-8, 14,15,19,20,23 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Horan et al. in view of Bischofberger et al. and prior art disclosed in the specification (page 30, lines 12-15).

The claims are drawn to a method for making lipidized proteins as per claims 4-6. Horan et al. teach lipidized glycoproteins including antibodies wherein the carbohydrate side chain of the glycoprotein is oxidized and a lipophilic amine is reacted to form a lipidized protein (see column 14, lines 39-46) and column 5, second paragraph. Horan et al. teach that said lipidized proteins can contain a radionucleotide (see column 7, second paragraph). Horan et al. teach the invention of claim 32 (see column 26, fifth paragraph). Horan et al. teach that the lipidized protein is made as per the methods of claim 1-3 (see column 14, lines 39-46). Antibodies are naturally occurring glycoproteins that are members of the immunoglobulin superfamily. Horan et al. teach the use of monoclonal antibodies in the claimed invention (see column 5, second paragraph). Horan et al. do not teach the claimed method wherein the lipoamines of claims 4-6 are used. Bischofberger et al. teach that an aminolipid (lipoamine) can be used for attaching a lipid

to an immunoconjugate (page 13, paragraph three). Bischofberger et al. teaches a wide variety of lipids can be used in the invention (page 4, third paragraph), and coupled with his previous teaching of a lipoamine for lipid conjugates, a routineer would have derived the lipoamine compounds of claims 4-6. The specification discloses that the lipoamines used in the method of claims 5 and 6 were known in the art (see page 30, lines 12-15). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Horan et al. teach lipidized glycoproteins including antibodies wherein the carbohydrate side chain of the glycoprotein is oxidized and a lipophilic amine is reacted to form a lipidized protein, the art recognizes that the lipoamines recited in claims 5 and 6 were known in the art and Bischofberger et al. teach that a variety of different aminolipid (lipoamine) can be used for attaching a lipid to an immunoconjugate.

37. No claim is allowed.

38. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 305-3014.

39. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Tuesday through Friday from 8:30 to 6:00. The examiner can also be reached on alternative Mondays. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP 1800 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1816
August ~~19~~ 26, 1996

973576

Application No.: 08/ ,

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: SEE ENCLOSED NOTE

Applicant Must Provide:

☐ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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